
A screen for drugs to protect against chemotherapy-induced hearing loss, using sensory hair cells derived by direct lineage reprogramming from hiPSCs

Grant Award Details

A screen for drugs to protect against chemotherapy-induced hearing loss, using sensory hair cells derived by direct lineage reprogramming from hiPSCs

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-11183

Investigator:

Name:	Neil Segil
Institution:	University of Southern California
Type:	PI

Disease Focus: Hearing Loss

Human Stem Cell Use: iPS Cell

Award Value: \$833,971

Status: Pre-Active

Grant Application Details

Application Title: A screen for drugs to protect against chemotherapy-induced hearing loss, using sensory hair cells derived by direct lineage reprogramming from hiPSCs

Public Abstract:**Research Objective**

Development of a screen using inner ear sensory hair cell-like cells made by direct lineage reprogramming, for discovering drugs to ameliorate hearing loss during cancer chemotherapy.

Impact

Hearing loss, both adult and pediatric, due to life-saving cisplatin chemotherapies. Lack of human inner ear hair cells for drug discovery purposes and disease modeling.

Major Proposed Activities

- Develop and optimize induced human hair cell-like cell screening technology for cisplatin ototoxicity (Aim 1), for use in otoprotectant screening (Aim 2) and disease modeling (Aim 3).
- Test previously identified otoprotectants (Vlastis et al., 2012) in human iHC screen with requisite otoprotective effects ("hits") against an LD50 dose of cisplatin (Aim 2).
- Screen a 2500-compound library of FDA-approved drugs (Enzo Life Sciences) in human iHC screen for requisite otoprotective effects ("hits") against an LD50 dose of cisplatin.
- Develop hair cell reporter lines from Cockayne Syndrome patient cells, and characterize human iHC disease models of cisplatin hypersensitivity in Cockayne Syndrome hair cells.
- Test whether otoprotectants identified in Aim 2 confer protection against cisplatin ototoxicity in human iHC disease models of ototoxicity hypersensitivity.

Statement of Benefit to California:

Cancer in both children and adults is frequently treated with chemotherapy agents that have a high potential to damage hearing. When this occurs in children, significant developmental delays require expensive rehabilitation and special education. Since regeneration does not occur, adults are frequently left with permanent hearing loss. This proposal uses state-of-the-art stem cell techniques to develop a screen to discover drugs that prevent hearing loss due to life-saving chemotherapy.

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